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THE EFFECTS OF EXHAUSTIVE EXERCISE ON RATS AT VARIOUS TIMES FOLLOWING BLAST EXPOSURE

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13. ABSTRACT

A series of four swim experiments using a 20° C. water bath was conducted with female, albino rats, Sprague Dawley strain. The purpose of the study was to: (1) investigate the effects of exhaustive exercise on rats at various times after exposure to airblast, (2) determine a time when exercise ceases to influence the mortality of blast-injured animals, and (3) estimate the recovery time required after blast trauma before maximum or near-maximal exercise capability is restored.

It was found that rats which were forced to swim to exhaustion as late as 1 hour following exposure exhibited a fourfold increase in lethality over nonexercised rats exposed to the same blast levels, and that exercise continued to exert an influence on blast lethality at 4 hours following exposure. However, the added stress of swimming did not increase lethality at 24 hours or 7 days. In addition, a near-normal swim performance was apparent at 7 days after traumatization.

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PREPARING AGENCY
Lovelace Foundation for Medical Education and Research
Albuquerque, New Mexico

FOREWORD

This report presents the results of studies conducted to investigate the effects of exhaustive exercise on blast-injured rats at various times following blast exposure in an effort to determine a time when exercise ceases to enhance lethality and when near-normal exercise capacity is restored.

Although the data are limited to results with rats, work of this type should be of interest to the military with respect to the establishment of adequate hazards criteria for combat troops. These findings should also be of interest to medical personnel from the standpoint of care of blast-injured subjects.

ABSTRACT

A series of four swim experiments using a 20° C. water bath was conducted with female, albino rats, Sprague Dawley strain. The purpose of the study was to: (1) investigate the effects of exhaustive exercise on rats at various times after exposure to airblast, (2) determine a time when exercise ceases to influence the mortality of blast-injured animals, and (3) estimate the recovery time required after blast trauma before maximum or near-maximal exercise capability is restored.

It was found that rats which were forced to swim to exhaustion as late as 1 hour following exposure exhibited a fourfold increase in lethality over non-exercised rats exposed to the same blast levels, and that exercise continued to exert an influence on blast lethality at 4 hours following exposure. However, the added stress of swimming did not increase lethality at 24 hours or 7 days. In addition, a near-normal swim performance was apparent at 7 days after traumatization.

ACKNOWLEDGMENTS

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The experimental work discussed in this manuscript was conducted according to the principles enunciated in the "Guide for Laboratory Animal Facilities and Care," prepared by the National Academy of Sciences-National Research Council.

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THE EFFECTS OF EXHAUSTIVE EXERCISE ON RATS AT VARIOUS TIMES FOLLOWING BLAST EXPOSURE

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INTRODUCTION

Exposure to the detonation of a nuclear device can result in a significant number of people with mixed forms of injuries produced by the combined effects of radiation, blast, and thermal components. Individuals so exposed may not be aware of the extent of their injuries until a considerable amount of time has elapsed. During this time, they may physically exert themselves in the performance of a task and, in so doing, may jeopardize their survival or recovery. The extent to which exercise influences survival or recovery from combined injuries has not been investigated. However, before a meaningful approach to the study of the effects of exertion on mixed forms of trauma can be established, baseline data must be collected to determine the influence of exercise on single forms of injuries resulting from radiation, blast, or thermal exposures.

Therefore, it was the purpose of this study to: (1) investigate the effects of exhaustive exercise on rats at various times following exposure to airblast, (2) determine a time when exercise ceases to influence the mortality of blast-injured animals, and (3) estimate the recovery time required after blast trauma before maximum or near-maximal exercise capability is restored.

MATERIALS AND METHODS

A total of 449 female, albino rats (Sprague Dawley strain), with a mean body weight of 201 (160-280) grams (g.), were used in this study. The animals were obtained, 110 at a time, from the Bio-Science Animal Laboratory, Oakland, California. Upon arrival in this laboratory, the animals were placed in pairs in wire cages and maintained at a room temperature of 24 $\pm$ 2° C. and at 45 $\pm$ 5 percent relative humidity. Purina Lab Chow and water were available ad libitum.

The study was divided into four experiments with the rats in these experiments designated for testing at 1 hour, 4 hours, 24 hours, and 7 days after blast exposure. Work was completed on one experiment before beginning the next.

Animals in an individual experiment were weighed and numbered on the left hip with miniaturized branding irons upon arrival in the laboratory. After a 1-week stabilization period, the rats were weighed and forced to swim, continuously and individually, to exhaustion in a 20° C. water bath. As described in reference 1, the animals were considered to be "exhausted" when they remained motionless below the water surface for an elapsed time of 10 seconds. However, if a rat started toward the surface at the end of this 10-second time period, she was allowed to regain the surface and continue the swim. Upon completion of the swim trial, the animal was removed from the water and placed in a cage containing cotton batting and allowed to dry under incandescent lamps. Swim times to exhaustion, designated as "baseline swims," were used as an index of exercise capability prior to blast exposure. The rats were then divided randomly into blast-only, blast-plus-swim, swim-only, and control animals. All animals were held for a minimum of 5 days before any further work was done with them.

The water bath utilized for swimming the rats was constructed from three aluminum tanks (52 x 26 x 27 inches), figure 1, each of which was separated into two sections by a divider so that as many as six animals could swim at one time. Water temperature was maintained at 20 $\pm$ 0.5° C. by thermostatically controlled heaters located in the outside tanks and a recirculating pump interconnected to all three tanks. Agitation of the water by the pump also helped in keeping the animals from floating. The water level was held at a constant

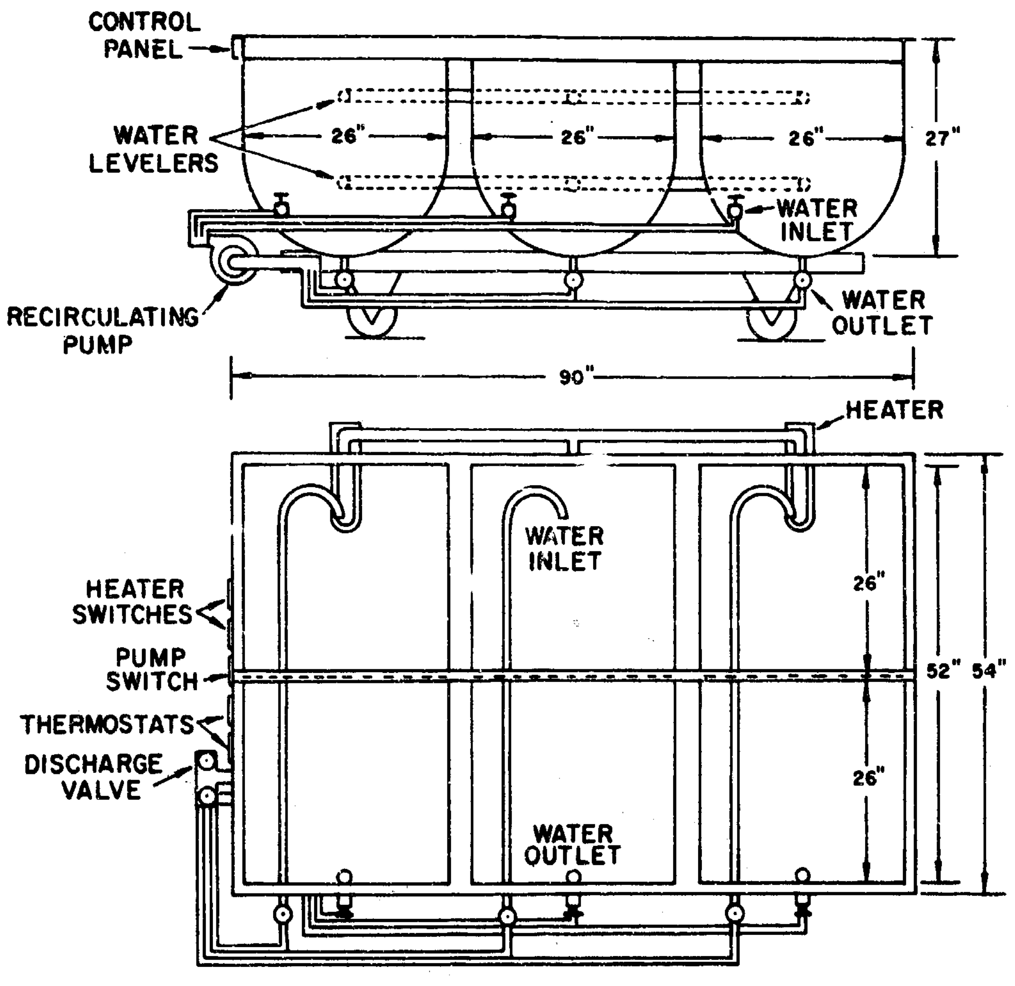

Figure 1. --Swim Tanks, Side View and Top View.

6 inches from the top of the tanks by a series of interconnecting tubes located at the top and the bottom of the tanks. At the end of each day of swimming, the tanks were drained and refilled with fresh water.

After the 5-day hold period, the rats were weighed and then exposed 12 at a time (six blast-only and six blast-plus-swim) to approximately LD_{30} levels of sharp-rising, long-duration overpressures generated by a 42-inch-diameter air-driven shock tube. This was accomplished by putting the rats in cone-shaped, chicken-wire cages and by randomly securing them to the endplate of the shock tube. Since the animals were secured to the endplate, the dose of interest was the reflected pressure. A description of the shock tube and instrumentation for pressure-time measurements has been reported in reference 2.

A series of five airblasts were required for one experiment. This resulted in 30 blast-only and 30 blast-plus-swim animals which were grouped with 30 swim-only animals. The remaining animals served as controls. If the mortality resulting from any one exposure was less than 8 percent or greater than 42 percent prior to the termination of the post-exposure hold time, the animals subjected to that overpressure and the corresponding swim-only animals were deleted from the group.

The rats were then held for the required post-exposure time after which both swim-only animals and blast-plus-swim animals were forced to swim to exhaustion. The animals utilized at 24 hours or 7 days after blast were again weighed prior to testing. In addition, the time of death and lung weights of the nonsurvivors were recorded whenever possible. The exceptions were those animals that died overnight. All of the remaining rats were sacrificed 7 days after the post-exposure swim date, and their lung weights were recorded.

Statistical analyses were done, when applicable, according to the methods described in reference 3. Estimations of significant difference in mortality were based on the 2 x 2 contingency tables presented in references 4 and 5.

RESULTS

Mortality

Exposure doses and mortality comparisons between rats subjected to blast alone and those subjected to blast and then swam to exhaustion at 1 hour, 4 hours, 24 hours, or 7 days afterwards are presented in table I. Graphical representations of percent mortality as a function of time after blast for the animals swam at 1 hour and 4 hours are shown in figure 2.

The data demonstrate that there was a significant ($p = 0.05$) enhancement in lethality of rats that were exercised 1 hour following injury. Approximately 58 percent of the blast-plus-swim animals died after 1 hour as compared to 14 percent for the blast-only subjects (Table I). The 24-hour mortality was 72 percent for the blast-plus-swim subjects and 33 percent for the blast-only subjects (Figure 2).

The animals that were exercised 4 hours after blast showed a slight increase in lethality over the nonexercised blast-exposed animals (Figure 2). The blast-plus-swim rats exhibited a 17-percent mortality after swimming as compared to no deaths after 4 hours in the corresponding blast-only rats (Table I).

No deaths occurred in animals that swam at 24 hours or 7 days after blast administration. There were also no deaths after these time periods in the blast-only animals (Table I).

Survival Times

The survival times of rats dying before and after exercise at 1 hour subsequent to injury and the survival times of nonexercised, blast-exposed rats from the same experiment are compared in table II. Animals that would have otherwise survived apparently died as the result of the imposition of the additional stress of exercise. This was demonstrated by the longer survival times of the blast-plus-swim animals. There were no exercised animals that died during the swimming, but there was one animal that was swam at 1 hour after blast that died 3 minutes after removal from the water (Table II).

TABLE I

MORTALITY COMPARISONS BETWEEN RATS EXPOSED TO BLAST ALONE AND THOSE EXPOSED TO BLAST AND THEN SWAM AT 1 HOUR, 4 HOURS, 24 HOURS, OR 7 DAYS AFTERWARDS

Time of Start of Exercise After Blast	Exposure Dose		Blast-Plus-Swim		Blast-Only	
	Mean Incident Pressure, p. s. i.	Mean Reflected Pressure, p. s. i.	Percent Deaths Prior to Exercise	Percent Deaths After Exercise	Percent Deaths Prior to Exercise of Blast and Swim Rats	Percent Deaths After Exercise of Blast and Swim Rats
1 hour	10. 5	30. 6	6/18 33. 3%	7/12 58. 3%	4/18 22. 2%	2/14 14. 3%
4 hours	10. 5	30. 2	6/24 25. 0%	3/18 16. 7%	6/24 25. 0%	0/18 0. 0%
24 hours	11. 1	31. 4	7/30 23. 3%	0/23 0. 0%	9/30 30. 0%	0/21 0. 0%
7 days	11. 8	31. 3	8/24 33. 3%	0/16 0. 0%	10/24 41. 7%	0/14 0. 0%

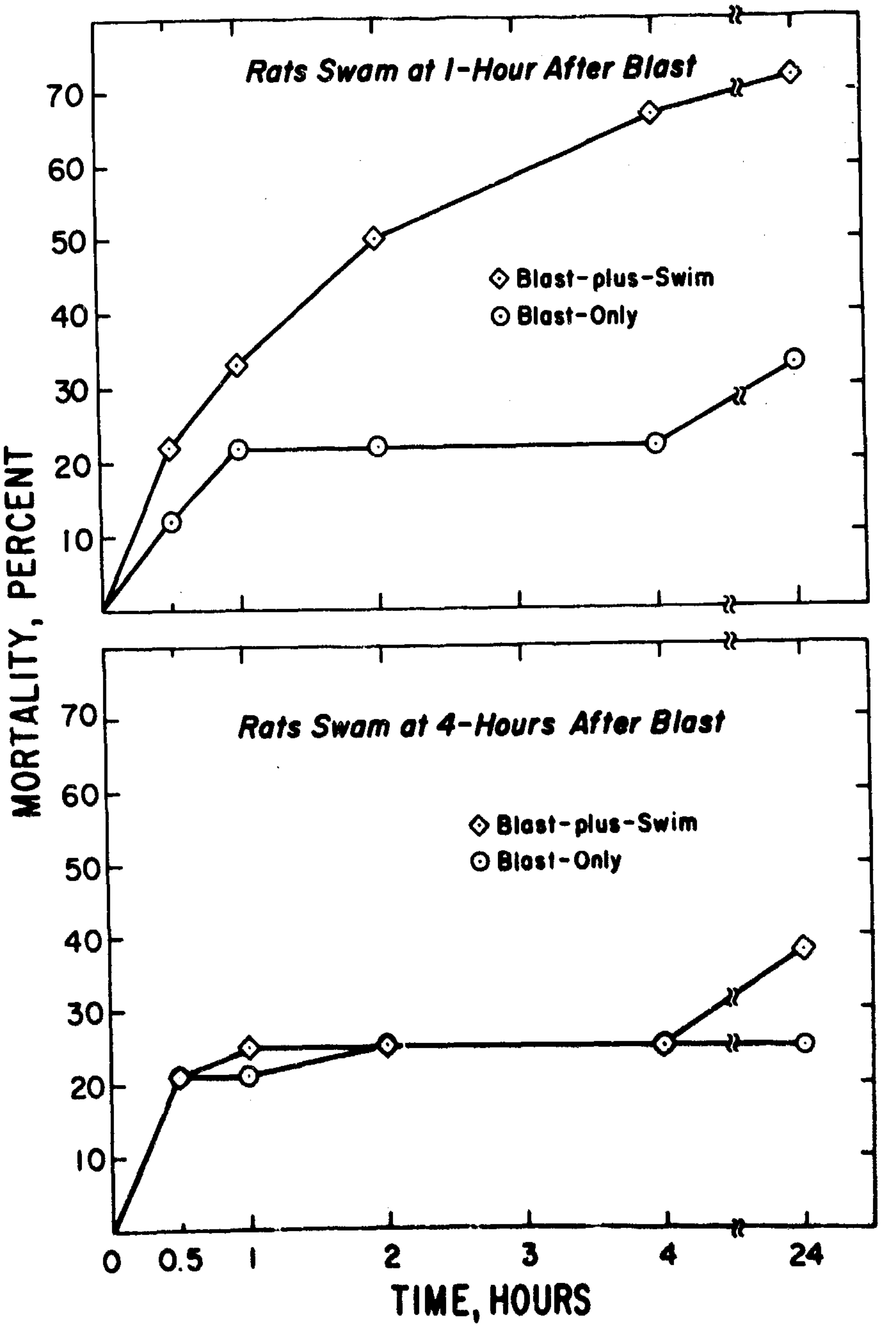

Figure 2. --Mortality as a Function of Time After Exposure for Rats Subjected to Blast Alone and Those Subjected to Blast and Then Swam at 1 Hour and 4 Hours Afterwards.

TABLE II

COMPARISON OF SURVIVAL TIMES OF ANIMALS SWAM AT 1 HOUR AFTER BLAST EXPOSURE

Animals Swam at 1 Hour After Blast				
Blast-Plus-Swim				Blast-Only
Survival Time After Exposure (min)	Survival Time Up to 1 hr (min)	Survival Time After 1 hr (min)	Survival Time After Swim (min)	Survival Time After Exposure (min)
99	-	39	19	34
73	-	13	3	DON[a]
44	44	-	-	DON[a]
154	-	94	80	2
190	-	130	114	2
240	-	180	148	4
44	44	-	-	-
110	-	50	33	-
2	2	-	-	-
1	1	-	-	-
7	7	-	-	-
7	7	-	-	-
DON[a]	-	DON[a]	DON[a]	-
81[b] (1-240)[c]	18 (1-44)	84 (13-180)	66 (19-148)	10 (2-34)

a. Animals which died overnight and were not included in estimate of mean.
b. Mean.
c. Range.

Performance Decrement

The mean baseline and mean post-exposure swim durations, the post-exposure swim times expressed as percentages of the baseline swim times, the adjusted percentages of the baseline swim times, and the performance decrements of the animals from the four experiments are given in table III. The performance decrement of the animals that were forced to swim to exhaustion after blast exposure was based on comparisons between the percents of baseline of the swim-only and blast-plus-swim animals of a particular experiment. It was assumed that the percent of the baseline swim time of the blast-plus-swim animals would have been similar to that of the swim-only animals if they had not been subjected to blast prior to swim. Those animals blasted and swam at 1 hour and 4 hours afterwards demonstrated 26- and 31-percent respective reductions in exercise capacity ($0.02<p<0.05$) and the animals that were forced to swim at 24 hours after blast exposure exhibited a 17-percent reduction in exercise capability ($0.1<p<0.2$). However, there was only a 10-percent loss in swim performance ($0.1<p<0.2$) of the animals that were forced to swim 7 days following blast administration (Table III).

The baseline, post-exposure, and a breakdown of the post-exposure swim times into swim times of survivors and those dying after swimming at 1 hour following blast are listed in table IV. The rats that survived both blast and swim, swam about as long as they did before blast injury. The animals that died after the post-exposure swim generally exhibited shorter swim times than their baseline times (Table IV).

Lung Weight, Percent of Body Weight

Table V presents the mean lung weights, expressed as percentages of the body weights, of the controls, the blast-only, and the blast-plus-swim animals from the experiment that was conducted 1 hour after blast. Animals that died after exercise demonstrated higher lung weights, 1.78 $\pm$ .10* percent, than those animals which died prior to exercise, 1.63 $\pm$ .06* percent.

*Standard error.

TABLE III

EFFECTS OF LD_{30} LEVELS OF AIRBLAST ON SWIM PERFORMANCE OF RATS

TABLE 3

EFFECTS OF LD_{30} LEVELS OF AIR BLAST ON SWIM PERFORMANCE OF RATS

Time of Start of Exercise After Blast	Treatment and Number of Subjects	Duration of Baseline Swim (min)	Duration of Second Swim (min)	Percent of Baseline	Adjusted Percent of Baseline[c]	Performance Decrement, (Percent)[d]
1 hour	Blast-Plus-Swim n = 12	32[a] (20-44)[b]	24 (10-46)	74 (32-113)	74	26 $0.02<p<0.05$[e]
	Swim-Only n = 18	34 (17-58)	33 (17-57)	100 (61-175)		
4 hours	Blast-Plus-Swim n = 18	40 (23-67)	23 (9-47)	59 (28-100)	69	31 $0.02<p<0.05$
	Swim-Only n = 24	41 (18-85)	33 (16-64)	90 (24-194)		
24 hours	Blast-Plus-Swim n = 23	25 (12-51)	22 (13-37)	97 (42-178)	83	17 $0.1<p<0.2$
	Swim-Only n = 30	28 (16-45)	31 (15-58)	114 (45-250)		
7 days	Blast-Plus-Swim n = 16	27 (18-39)	23 (14-34)	85 (51-107)	90	10 $0.1<p<0.2$
	Swim-Only n = 23	30 (19-45)	28 (14-49)	95 (59-127)		

a. Mean.

b. Range.

c. Adjusted Percent of Baseline = Percent of Baseline of Blast-Plus-Swim + (100-Percent of Baseline of Swim-Only)

d. Performance Decrement = 100 - Adjusted Percent of Baseline.

e. Probability of significant difference determined by t-test for unpaired variates between the percents of baseline of the blast-plus-swim and swim-only animals.

TABLE IV

SWIM PERFORMANCE AS A FUNCTION OF SURVIVORSHIP

Rats Swam 1 Hour After Blast			
Baseline[a] Swim Time (min)	Post-Exposure Swim Time (min)	Swim Time of Survivors (min)	Swim Time of Deaths (min)
44	46	46	-
41	20	-	20
31	10	-	10
34	14	-	14
41	42	42	-
39	16	-	16
32	32	-	32
29	18	18	-
20	17	-	17
20	13	-	13
24	22	22	-
30	34	34	-
32[b] (20-44)[c]	24 (10-46)	32 (18-42)	17 (10-32)

a. Swim times of animals dying prior to swimming at 1 hour after exposure are not listed.
b. Mean.
c. Range.

TABLE V

COMPARISON OF LUNG WEIGHTS OF RATS RECEIVING NO BLAST TO THOSE THAT WERE SUBJECTED TO SWIMMING 1 HOUR AFTER BLAST EXPOSURE AND THEIR COUNTERPARTS WHICH WERE BLASTED AND NOT FORCED TO SWIM

	Lung Weight, Percent of Body Weight			
	Controls	Survivors [a]	Deaths Before 1 hr	Deaths After 1 hr [b]
n	10	17	9	6
Mean	0.55	0.83	1.63	1.78
Range	(0.49–0.63)	(0.68–0.96)	(1.33–1.91)	(1.40–2.05)
S. D.	.06	.08	.18	.25
S. E.	.02	.02	.06	.10

a. Survivors sacrificed 7 days following exposure and comprised of animals subjected to blast only and those subjected to blast and swimming.

b. All animals in this group died after swimming.

DISCUSSION

The results of this study demonstrate that strenuous exercise occurring soon after exposure to LD_{30} levels of airblast enhances lethality and that this potentiating effect decreases as a function of time after injury. Rats that were forced to swim 1 hour following initial insult exhibited a fourfold increase in lethality over nonexercised rats that received the same blast dose. This effect on mortality is also apparent at earlier times following blast (Reference 6) and continues to exert an influence on lethality up through 4 hours. The stress associated with the exhaustive exercise does not enhance lethality at 24 hours, and this lack of enhancement is also apparent at 7 days (Table I).

These changes in the influence of exercise on lethality with time are possibly related to the rate of resolution of lung hemorrhage and edema. The previously unpublished data, presented in figure 3, indicate that the mean lung weight of rats, expressed as percent of the body weight, decreases as a function of time after blast injury to near the control level at 7 days, and that the major reduction in lung weight occurs during the first 24 hours following the initiation of the injury. These data were obtained from the survivors of five groups of rats that were sacrificed at 15 minutes, 1 hour, 4 hours, 24 hours, and 7 days after exposure to blast doses equivalent to those utilized in this study. In reference 7, it was shown that the resolution of lung hemorrhage occurs at a strikingly rapid rate and, more strikingly, that disrupted parenchymal tissue is nearly restored to normal with the possible exception of residual hypertrophy of small branches of the pulmonary artery and frequently observed thickenings of alveolar septa. There was no gross evidence of pulmonary hemorrhage beyond 10 days; however, tissue edema, atelectases, emphysema, and plethora were noted in the lungs of survivors out to 60 days. In addition, it has been indicated in studies with blast-injured sheep that marked improvement in pulmonary function occurs within the first 24 hours following blast exposure and that the increased venous admixture attendant with pulmonary damage is back to near-normal levels 7 days after injury (Reference 8).

Animals that survive blast run the risk of continued hemorrhage and edema from disrupted parenchymal tissue during the first few hours of recovery

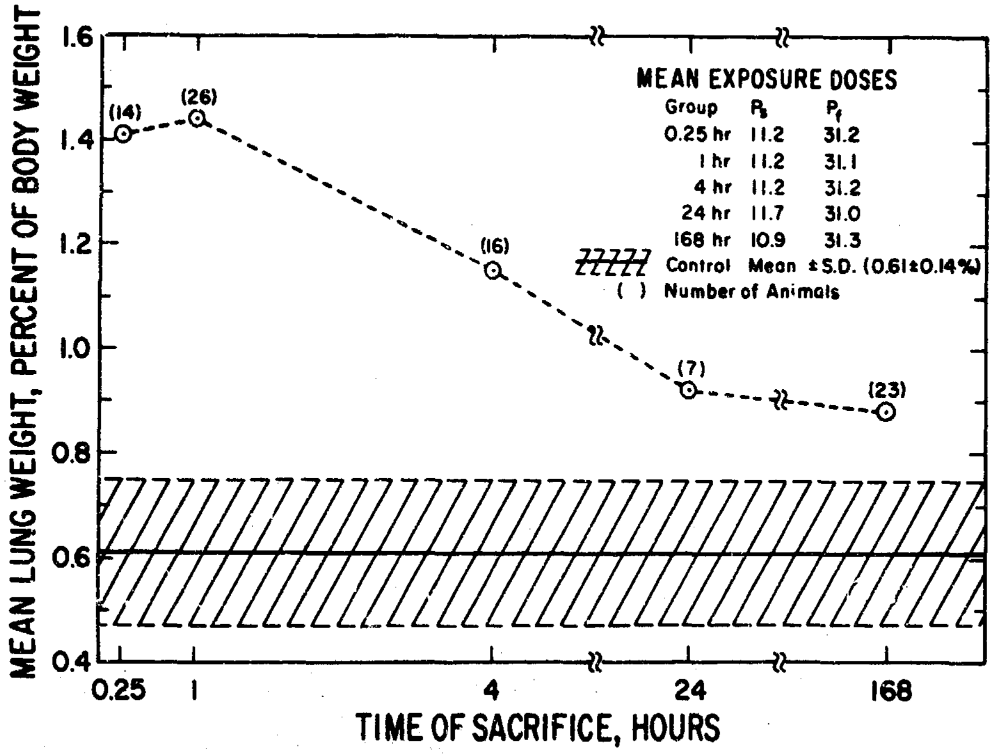

Figure 3. --Mean Lung Weights of Rats Which Were Sacrificed At Various Time Intervals After Blast. (P_s = Incident Pressure, p. s. i.; P_f = Reflected Pressure, p. s. i.)

(Reference 9). The stress of exercise possibly increases this risk. The mean percent lung weight of the rats that died after swimming at 1 hour subsequent to blast is higher than that of the animals that were exposed to similar blast doses and sacrificed at 1-hour post-exposure (Table V and Figure 3). The stress associated with exercise and additional pulmonary hemorrhage might also aggravate the existing anoxic pulmonary hypertension and acute cor pulmonale; thereby precipitating pulmonary edema, further anoxia, uncompensated metabolic and respiratory acidosis, progressive right heart failure, cardiac fibrillation, and death (References 7 and 10).

Recovery from blast injury has proceeded to such a point in the rat that at 24 hours exercise can be undertaken without the apparent risk of death but has not proceeded to the point that maximal exercise capability is restored (Table III). However, exercise capability is restored to near-normal levels at the end of 7 days (Table III).

The general adaption syndrome described in reference 11 may enchance the exercise capability of blast-injured animals, particularly those sustaining non-lethal lung injury; and this may be a plausible explanation for the swim performance of the blast-plus-swim survivors in the 1-hour experiment (Table IV). Three out of five of the animals swam longer after being traumatized than they did before.

In view of the results of this study, the following statements could be made with regard to the care of blast casualties. Complete inactivity should be mandatory for at least 24 hours subsequent to injury. This would in effect reduce the workload on the cardiopulmonary system, thereby minimizing the chances of further pulmonary hemorrhage, edema, and heart failure (Reference 9). After 24 hours, activity should still be restricted for at least a period of a week. According to reference 10, recurrence of lung hemorrhage ha[illegible]n recorded in human casualties up to 5 days and periodic hemoptysis as long as 7 to 10 days following injury.

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